Editorial

Potential Benefits of Combining Multisite Pacing and ICD Therapy for Hemodynamic and Antiarrhythmic Results

B. MERKELY
Department of Cardiovascular Surgery, Semmelweis University, Budapest, Hungary

Summary

Multisite pacing techniques have recently been developed either for hemodynamic or antiarrhythmic results. These new modalities aim to decrease the degree of atrial and/or ventricular electromechanical asynchrony. Biventricular pacing has been proposed in patients with severe, drug-refractory heart failure associated with a significant intraventricular conduction delay. New clinical data suggest that biventricular pacing has antiarrhythmic effects as well. Dual-chamber implantable cardioverter defibrillator (ICD) therapy combined with biatrial pacing and a coronary sinus shock electrode may be useful in patients with paroxysmal atrial fibrillation and ventricular tachyarrhythmias. Multisite pacing and ICD therapy might have synergistic benefits. However, the antiarrhythmic mechanism of multisite pacing is not well understood and prospective randomized trials are needed to identify those patients who will best respond to this type of therapy.

Key Words

Multisite pacing, biatrial and biventricular stimulation, implantable cardioverter-defibrillator (ICD)

Introduction

Multisite pacing can be defined as pacing or sensing from more than one site in a given chamber, whether in the atrium or the ventricle. Pacing from both the right and left ventricles (or atria) is called biventricular (or biatrial), multichamber pacing. However, multichamber pacing is also often called multisite pacing. The aim of multisite pacing is the electromechanical resynchronization of cardiac function.

Multisite Atrial Pacing and ICD

Multisite atrial (dual-site right atrial, biatrial, or standard right atrial and coronary sinus left atrial) pacing modes have been reported to be effective in the prevention of atrial fibrillation (AF) [1-4]. Multisite atrial pacing is superior to single right atrial pacing in the prevention of recurrent AF [3-5]. Biatrial pacing has been demonstrated to increase arrhythmia-free intervals in patients with frequent, drug-refractory, paroxysmal AF. The antiarrhythmic mechanism of multisite atrial pacing is not well understood and is likely related to atrial electromechanical resynchronization, resulting in a decrease of P-wave duration. In one experimental study, the effects of single-, dual-, triple-, and quadruple-site atrial pacing or atrial activation and refractoriness were determined in normal canine hearts. Activation times and local recovery intervals were minimized by triple-site stimulation, whereas a

fourth site did not result in further shortening. Septal stimulation produced epicardial activation times comparable to quadruple-site stimulation. Local refractory periods and their dispersion always remained unaffected. Functional conduction blocks apparent during single-site pacing were found to resolve during multisite stimulation [6]. Multisite pacing can prevent functional conduction blocks through multidirectional excitation and a reduction in total activation time. In spite of unaffected local refractory periods, the shortening of local recovery intervals might homogenize atrial repolarization and, thus, contribute to the preventive effects of multisite pacing [6].

The possible role of inhibition or "normalization" of atrial remodeling in the antiarrhythmic mechanism should also be taken into account. In some cases, the antiarrhythmic effect appears after several weeks or months. A decrease in the number of left atrial premature beats during biatrial pacing, experienced in some of our patients, could be caused by altered atrial electrophysiologic properties [7]. By reducing the number of atrial premature beats, the trigger for AF will be eliminated (reentry and focal activity). Biatrial pacing can also improve the hemodynamics by using an optimal left atrioventricular (AV) interval.

Dual-chamber implantable cardioverter defibrillator (ICD) therapy combined with biatrial pacing and a coronary sinus shock coil may be useful in patients with paroxysmal AF and ventricular tachyarrhythmias. The crucial feature of this device is the capability of both synchronous dual-chamber and biatrial pacing along with dual-chamber tachyarrhythmia detection and therapy [8]. High-frequency burst and low energy cardioversion using the coronary sinus shock coil can reduce the AF duration. Shortening the attacks of AF may exert an antiarrhythmic effect by limiting electrical, anatomical, and neurohumoral remodeling.

Several unanswered questions remain for future consideration. The role of biatrial pacing in congestive heart failure or bradycardia is not clearly identified, and neither is the question whether prolongation of the P-wave duration is acceptable as an indication criterion for biatrial pacing. Further questions concern the optimal location of the right and left atrial electrodes and the relevance of an intraoperative electrophysiologic study in the evaluation of responding patient groups (inter-, intraatial conduction time, inducibility of AF).

According to the most widely accepted recommendations, a biatrial pacemaker implantation is indicated in patients with frequent, drug-refractory, paroxysmal lone or non-valvular AF, if intra- and/or interatrial conduction disturbances are simultaneously present.

Biventricular Pacing and ICD

The purpose of multisite, biventricular pacing is AV synchronization and restoration of ventricular relaxation and contraction sequences by pacing both ventricles simultaneously at specific sites. Optimizing the AV delay can diminish AV regurgitation and lengthen the ventricular filling time [9]. Intra- and interventricular resynchronization, resulting from a decrease of QRS duration, restores the ventricular contraction sequence and reduces septal dyssynchrony.

Mostly acute changes of hemodynamic and clinical parameters during biventricular pacing have been investigated. Some investigators found a decrease of presystolic mitral regurgitation and pulmonary capillary wedge pressure, or an increase in cardiac index or an improvement in NYHA functional class [10,11]. Chronic effects of biventricular pacing can be an improvement in NYHA functional class, improvements in the patient's quality of life and a six-minute walking distance, an increase in peak oxygen uptake, and, in some cases, a decrease in left ventricular endsystolic and enddiastolic diameter [12,13]. The MUSTIC study investigated the clinical efficacy and safety of transvenous, atrio-biventricular pacing in patients with severe heart failure and major intraventricular conduction delay but without standard indications for a pacemaker. This single-blind, randomized, controlled crossover study compared the responses of patients during two periods: a 3-month period of active (atrio-biventricular) and inactive (ventricular inhibited at a basic rate of 40 beats/min) pacing. The results of the MUSTIC study demonstrated that the mean distance walked in 6 min was greater with active pacing, the quality-of-life score improved, peak oxygen uptake increased, hospitalizations were decreased, and active pacing was preferred by 85 % of the patients [13].

The potential antiarrhythmic effect of biventricular pacing may be associated both with improving hemodynamic status and direct electrophysiologic effects. There are several potential mechanisms: a decrease in ventricular conduction delays with biventricular pacing, contributing to a decrease in macro-reentry, avoid-

ance of pause-dependent tachyarrhythmias, and a decrease in plasma catecholamine levels with biventricular pacing [14]. Slight overdrive pacing may provide a further antiarrhythmic effect. In a randomized crossover study, biventricular pacing significantly decreased 24-hour ventricular ectopic count and ventricular salvo count, as measured by Holter monitoring, compared to no pacing [15]. In addition to electromechanic resynchronization, long-term biventricular pacing can inhibit ventricular remodeling, thus leading to a further decrease in arrhythmogenesis. One study investigated the effects of acute biventricular pacing on sustained ventricular tachycardia (VT) inducibility. The main finding of this study was that acute biventricular pacing decreased the inducibility of sustained monomorphic VT in patients with ischemic cardiomyopathy. Sustained VT could not be induced with biventricular pacing in 71 % of patients in whom VT was induced at baseline with standard programmed electrical stimulation [16].

Congestive heart failure is often combined with permanent AF. Some data suggest that patients with left bundle branch block (LBBB) and chronic AF can benefit from ventricular resynchronization alone, without AV-delay optimization. Up to 20 – 41 % of patients with non-ischemic cardiomyopathy have an inter- and/or intraventricular conduction delay. More than 90 % of patients with wide QRS have LBBB, and these patients have a poor prognosis. A leading cause of death in patients suffering from severe heart failure is sudden death mediated by malignant ventricular arrhythmia. It is increasingly likely that heart failure patients with poor functional status at high risk for sudden death will be considered for both an ICD and a biventricular pacemaker.

Despite the early promising experiences with biventricular pacing, there are some disadvantages to triple-chamber pacing. Implantation usually takes several hours, the risk of surgical complications and lead dislocation is relatively high, and there is a risk of injury from the three leads located in the same vein. Furthermore, it is uncertain whether biventricular pacing is superior to left ventricular pacing alone. Some investigators found that acute, single-site, left ventricular pacing was equal or superior to biventricular pacing in patients with congestive heart failure and LBBB [17-20].

Further open questions regarding biventricular pacing are those related to the optimal pacing site (lateral, posterior, or anterior) and the role of biventricular pacing in chronic AF or in moderate heart failure (NYHA II); long-term results are also needed. Currently, there is no proper guideline with biventricular pacemaker indications, which is caused by the lack of randomized studies with long-term follow-up and mortality endpoint. Heart failure patients with NYHA III-IV functional classes, sinus rhythm, and wide QRS complexes longer than 150 ms duration in the presence of LBBB seem to benefit most from biventricular pacing. A combination of biventricular pacing and ICD therapy might offer synergistic benefits. Class I or IIB ICD indication allows combined biventricular and ICD therapy in patients with the above-mentioned criteria. Any lingering questions on multisite pacing can be answered both by experimental and randomized crossover clinical studies.

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Contact
Béla Merkely, MD, PhD
Department of Cardiovascular Surgery
Semmelweis University
Városmajor u. 68
Budapest XII
H-1122 Hungary
Telephone: +36 1 355 4984
Fax: +36 1 355 4684
E-mail: merkbel@hermes.sote.hu